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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/707,994	01/30/2004	Roger Ariel Alberto	1292.1	1993

24289 7590 07/22/2008

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
07/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Response to the Amendment

The Amendment filed on 6/04/2008 in response to the previous Final Office Action (04/04/2008) is acknowledged and has been entered.

Claims 22-53 are currently pending and under consideration.

Rejections Withdrawn:

The rejection of Claims 22-39, 43-48 and under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter is withdrawn in view of Applicants arguments found on page 3, 2nd full paragraph of the remarks.

Rejections Maintained:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 22-29, 32-37 and 40-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Mattes (US 5,759,514, 1994).

Mattes teaches a conjugate comprising a tumor targeting protein or polypeptide linked to a radiolabeled nucleic acid-targeting small molecule, wherein the small molecule, after being liberated from the targeting protein by intracellular enzymes endogenous to the targeted tumor cell, is capable of passing through the lysosomal and nuclear membranes and intercalating a nuclear component (column 1, lines 49-56). With regards to the tumor targeting protein, the patent teaches that tumor targeting proteins include, but are not limited to, antibodies (column 2, lines 63-66). With regards to the nucleic acid small molecule, the patent teaches that nucleic acid small molecules include, but are

not limited to, acridine and derivatives thereof, as well as phenanthridines (column 2, liens 41-61). With regards to the radiolabel, the patent teaches that the radiolabels include, but are not limited to, ^{188}Rh (column 2, line 40). Moreover, the patent teaches a method of treating a patient having a tumor comprising the step of administering to the patient a therapeutically effective amount of the aforementioned therapeutic anti-tumor conjugate (column 2, lines 13-16).

In response to this rejection, Applicants contend that the present claims recite, inter alia, "a metal complexed with the intercalating moiety." Thus, Applicants submit that although it is not intended or suggested that the specification should be read into the present claims, Applicants submit that the specification may be used as a guide for the claims. In the present case, Applicants assert that Examples of metals complexed with intercalating moieties are provided in Figures 2 and 3, which clearly shows that the intercalating moiety is part of a coordination complex attached to the metal species at multiple points (multi-dentate) to form a metal complex, wherein the metal complexes formed are stable, both in vitro and in vivo. In contrast, Applicants assert that Mattes teaches a radiolabeled nucleic acid-targeting small molecule, wherein the radioactive atoms are covalently bound to a single carbon on the small molecule; and therefore, are not metal complexes. Thus, Applicants contend that although Mattes discloses a list of radionuclides, including two metals, which are claimed to work as radiolabels, Mattes discloses no multi-dentate ligands or synthesis procedures that may be used to form stable metal complexes with these metals. Hence, according to legal precedent, Applicants contend Mattes can not anticipate the claimed invention since the reference must disclose the identical invention in as complete detail as in the claims to support a prima facia case for anticipation.

These arguments have been carefully considered, but are not found persuasive.

In the instant case, the Examiner has carefully considered Applicants arguments and has carefully reviewed Applicants specification. However, the Examiner recognizes that the instant claims recite "[A] compound comprising: a moiety having an affinity for cancer cells; an intercalating moiety coupled to the moiety having an affinity for cancer cells, wherein the intercalating moiety comprises at least one unsubstituted aromatic ring that shares two carbons with only one other aromatic ring, and is configured to insert into the structure of deoxyribonucleic acid; and a metal complexed with the intercalating moiety." Thus, the claims do not appear to require the limitation of the intercalating moiety being "multi-dentate ligand" nor do the claims appear to require the

limitation of the intercalating moiety being coordinated though more than one bond to the metal, as asserted by Applicants. In addition, the Examiner acknowledges and does not dispute Applicants submission that that the specification may be used as a guide for the claims. However, the Examiner recognizes that during examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, 367 F.3d 1359, 1369, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004). In the instant case, with the exception of the compounds disclosed in Figures 2 and 3, the specification appears to be silent on a definition of a complex. Therefore, the Examiner must give claims their broadest reasonable interpretation, in light of the specification which means that the words of the claim must be given their plain meaning unless the plain meaning is inconsistent with the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). The word complex, as defined by Encarta "On Line Dictionary", in chemistry relates to a compound in which nonmetal molecules or ions form weak bonds, **coordinate bonds,** with a central metal atom. Thus, the definition does not appear to limit the complex to having more than one bond. As such, a single bond formed between the intercalating moiety and metal still appears to meet the definition of a complex.. With regards to Applicants assertions that Mattes does not teach the synthesis or stability of the claimed product, the Examiner recognizes that the patentability of a product does not depend on its method of production. If the product is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 30-31 and 38-39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mattes (US 5,759,514, 1994), as applied to claims 22-29, 32-37 and 40-53 above, in view of Holley et al. (Cancer Research 1992; 52: 4190-4195, of record).

Mattes teaches a conjugate comprising a tumor targeting protein or polypeptide linked to a radiolabeled nucleic acid-targeting small molecule, wherein the small molecule, after being liberated

from the targeting protein by intracellular enzymes endogenous to the targeted tumor cell, is capable of passing through the lysosomal and nuclear membranes and intercalating a nuclear component (column 1, lines 49-56). With regards to the tumor targeting protein, the patent teaches that tumor targeting proteins include, but are not limited to, antibodies (column 2, lines 63-66). With regards to the nucleic acid small molecule, the patent teaches that nucleic acid small molecules include, but are not limited to, acridine and derivatives thereof, as well as phenanthridines (column 2, liens 41-61). With regards to the radiolabel, the patent teaches that the radiolabels include, but are not limited to, ^{188}Rh (column 2, line 40). Moreover, the patent teaches a method of treating a patient having a tumor comprising the step of administering to the patient a therapeutically effective amount of the aforementioned therapeutic anti-tumor conjugate (column 2, lines 13-16).

Mattes does not explicitly teach that tumor seeking molecule is spermidine.

Holley et al. teach a method of targeting chlorambucin to a tumor cell by conjugating chlorambucin to spermidine (page 4191, 1st column, 1st full paragraph). In particular, the reference teaches that the chlorambucin-spermidine conjugate showed greater anti-tumor activity both in vivo and in vitro compared to chlorambucin due to increased tumor uptake and increased affinity for DNA (page 4194, 2nd column, last paragraph)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the conjugate taught by Mattes. with a spermidine in view of the teachings Holley et al.. One would have been motivated to so because Holley et al. teach that spermidine conjugates show increase tumor uptake and increased affinity for DNA. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by modifying the conjugate taught by Mattes with a spermidine in view of the teachings Holley et al, one would achieve a targeted radioactive immunoreagent for the treatment and diagnosis of a tumor.

In response to this rejection, Applicants assert that, as discussed with respect to the rejection under 35 USC 102, Mattes does not disclose "a metal complexed with the intercalating moiety," as recited in claims 22 and 32 and Holley, either individually or in any sort of hypothetical combination, doe snot obviate this deficiency. As such, Applicants assert that claims 22 and 32 are allowable over Mattes in view of Holley.

These arguments have been carefully considered, but are not found persuasive for the reasons set forth above and incorporated herein.

Therefore, NO claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf
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Art Unit 1642

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